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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/801,380	03/15/2004	Iddys D. Figueroa	200315726-1	3172

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EXAMINER	
SASAN, ARADHANA	
ART UNIT	PAPER NUMBER
1615	
MAIL DATE	DELIVERY MODE
05/12/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/801,380	FIGUEROA ET AL.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18, 32-45 and 49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18,32-45 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 3/19/08 are acknowledged.

2. Claims 1-3 were amended. New claim 49 was added.

3. Claims 1-18, 32-45 and 49 are included in the prosecution.

Response to Arguments

Rejection of claims 1, 3-4, 8, 15, 18, 32-33 and 38-46 under 35 USC § 102(b)

4. Applicant's arguments, see Page 7, filed 3/19/08, with respect to the rejection of claims 1, 3-4, 8, 15, 18, 32-33 and 38-46 under 35 USC § 102(b) as being anticipated by Voss et al. (US 4,322,449) have been fully considered but are not found persuasive.

Applicant argues that nothing in Voss expressly discloses a target dissolution rate based on one or more deposition characteristics, an application parameter, or dot size. Applicant argues that the Examiner appears to be arguing that control of dissolution rate and dosing are one and the same, which is simply not the case. Applicant argues that Voss does not describe the use of deposition characteristics or application parameters as a means of controlling dissolution rate, much less suggest that these variables are even a factor in determining dissolution rate. Applicant states that Voss is primarily concerned with applying a specific volume of liquid on to a surface, regardless of dissolution rate. Applicant argues that it does not follow that the dosing of active pharmaceutical ingredients taught in Voss will necessarily result in control of dissolution rate. Applicant argues that one of ordinary skill in the art would understand that the technology taught in Voss would not be capable of the precision

and control of deposition characteristics necessary for controlling or attaining a target dissolution rate.

This is not found persuasive because in order to achieve "extremely precise dosing of active pharmaceutical ingredients" a skilled artisan would ensure that the effective dose of the active and process parameters such as volume of drops and dot size enabled the target dosing. The target dissolution rate is inherently a function of the dose, i.e. the dose size, the dose volume, the rate of dotting on a substrate etc. It is inherent that deposition characteristics will be used to ensure precise deposition of active ingredients.

Applicant submits that Voss discloses only use of continuous ink ejectors, an old technology. This is not found persuasive because Voss teaches "extremely precise dosing of active pharmaceutical ingredients" regardless of old technology.

Therefore, the rejection of 12/19/07 is maintained.

Rejection of claims 2, 5-7, 9-14, 16-17, and 35-37 under 35 USC § 103(a)

5. Applicant's arguments, see Page 9, filed 3/19/08, with respect to the rejection of claims 2, 5-7, 9-14, 16-17, and 35-37 under 35 USC § 103(a) as being unpatentable over Voss et al. (US 4,322,449) in view of Stimpson et al. (BioTechniques 25:886-890 November 1998) have been fully considered but are not found persuasive.

Applicant argues that Voss does not teach each and every element, either expressly or inherently of claims 1, 4, and 32 because Voss does not teach or suggest a target dissolution rate, rather, Voss is solely concerned with overall exact dosing of

pharmaceuticals, and as such, Voss does not teach, inherently or expressly, all the claim limitations.

This is not found persuasive because as discussed above Voss anticipates the limitation of achieving target dissolution rate.

Applicant argues that Stimpson does not have anything to do with a target dissolution rate and contrary to claims 1, 4, and 32, Stimpson desires the printed DNA lines to remain on the print medium rather than control or attain target dissolution rate.

This is not found persuasive because Stimpson is used as a supporting reference that provides the teaching of thermal ink jet dispensing of active agents. Stimpson is used in combination with Voss which teaches extremely precise dose dotting of actives and inherently teaches selecting the target dissolution rate. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Therefore, the rejection of 12/19/07 is maintained.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 3-4, 8, 15, 18, 32-33, and 38-46 remain rejected and new claim 49 is rejected under 35 U.S.C. 102(b) as being anticipated by Voss et al. (US 4,322,449).

The claimed invention is a method of controlling a dissolution rate of a bioactive agent comprising selecting a target dissolution rate and applying a bioactive agent to a delivery substrate as a plurality of substantially uniformly sized dots to attain the selected target dissolution rate.

Voss discloses "a method for the preparation of pharmaceuticals which comprises using a piezoelectric dosing system to dot liquid, dissolved or suspended active substance onto a pharmaceutical carrier" (Abstract). "Extremely precise dosing of active pharmaceutical ingredients onto pharmaceutical carriers can be achieved if the liquid, dissolved or suspended active substance is dotted onto the pharmaceutical carrier in a specific quantity in the form of discrete droplets of specific volume. The dotting is effected by, for example, means of tubular or plate-shaped piezoelectric dosing systems" (Col. 1, line 62 to Col. 2, line 1). "The process of dosed dotting of pharmaceutical carriers opens up the possibility of exact dosing of active substance …" (Col. 6, lines 8-11).

Regarding instant claim 1, the limitation of applying a bioactive agent to a delivery substrate as a plurality of substantially uniformly sized dots is anticipated by the teaching of the active substance dotted onto the pharmaceutical carrier in a specific quantity in the form of discrete droplets of specific volume as taught by Voss (Col. 1, lines 62-67). The limitation of selecting a target dissolution rate is an inherent feature of the "extremely precise dosing of active pharmaceutical ingredients" because the ability

to achieve “extremely precise dosing” of an active agent onto the “pharmaceutical carrier” (reads on the instant delivery substrate) is possible only when one predetermines how much to add before dosing. Since the limitation of selecting a target dissolution rate and the limitation of applying a bioactive agent to a delivery substrate as a plurality of dots is anticipated by Voss, the method of controlling a dissolution rate of a bioactive agent (comprising these limitations) is also anticipated by Voss.

Regarding instant claims 3, 15 and 38, the limitation of displacing a solution including the bioactive agent with a piezoelectric ejection element is anticipated by the piezoelectric dosing system disclosed by Voss (Col. 1, line 67 to Col. 2, line 1).

Regarding instant claim 4, the limitation of applying a bioactive agent to a delivery substrate in drops of solution configured to form dots is anticipated by the teaching of the active substance dotted onto the pharmaceutical carrier in a specific quantity in the form of discrete droplets of specific volume as taught by Voss (Col. 1, lines 62-67). The limitation of selecting a desired dot size is an inherent feature of the “extremely precise dosing of active pharmaceutical ingredients” because the ability to achieve “extremely precise dosing” of an active agent onto the “pharmaceutical carrier” (reads on the instant delivery substrate) is possible only when one predetermines how much to add (i.e. the desired dot size) before dosing. Since the limitation of selecting a desired dot size and the limitation of applying a bioactive agent to a delivery substrate in drops of solution is anticipated by Voss, the method of controlling a dissolution rate of a bioactive agent (comprising these limitations) is also anticipated by Voss.

Regarding instant claim 8, the limitation of "substantially uniformly sized" dots is anticipated by the "discrete droplets of specific volume" taught by Voss (Col. 1, lines 62-67).

Regarding instant claim 18, the concentration of the bioactive agent in the solution set to form dots having the desired dot size on the delivery substrate is anticipated by the teaching of the active substance dotted onto the pharmaceutical carrier in a specific quantity in the form of discrete droplets of specific volume as taught by Voss (Col. 1, lines 62-67). The limitation of setting the concentration of the bioactive agent is an inherent feature of the "extremely precise dosing of active pharmaceutical ingredients" because the ability to achieve "extremely precise dosing" of an active agent onto the "pharmaceutical carrier" (reads on the instant delivery substrate) is possible only when one predetermines how much to add (i.e. sets the concentration of the bioactive agent) before dosing.

Regarding instant claim 32, the limitation of setting an application parameter based on a target dissolution rate is an inherent feature of the "extremely precise dosing of active pharmaceutical ingredients" because the ability to achieve "extremely precise dosing" of an active agent onto the "pharmaceutical carrier" (reads on the instant delivery substrate) is possible only when one establishes the appropriate application parameters (such as nozzle size) in order to achieve the desired dosing and dissolution rate. The limitation of applying a bioactive agent to a delivery substrate according to the application parameter to achieve the target dissolution rate is anticipated by the teaching of the active substance dotted onto the pharmaceutical carrier in a specific

quantity in the form of discrete droplets of specific volume as taught by Voss (Col. 1, lines 62-67). Since the limitation of setting an application parameter and the limitation of applying a bioactive agent to a delivery substrate according to the application parameter is anticipated by Voss, the method of controlling a dissolution rate of a bioactive agent (comprising these limitations) is also anticipated by Voss.

Regarding instant claims 33-34, the limitation of ejecting an ejection solution including the bioactive agent onto the delivery substrate as a plurality of drops and the limitation of the "sized" drops is anticipated by the teaching of the active substance dotted onto the pharmaceutical carrier in a specific quantity in the form of discrete droplets of specific volume as taught by Voss (Col. 1, lines 62-67).

Regarding instant claim 39, the limitation of an ejection solution including the bioactive agent and a carrier solvent is anticipated by the teaching of the liquid, dissolved or suspended active substance that is dotted onto the pharmaceutical carrier as taught by Voss (Col. 1, lines 62-67).

Regarding instant claims 40-46 and 49, the limitations of the deposition characteristic and the limitations of the application parameter are inherent features of the "extremely precise dosing of active pharmaceutical ingredients" as taught by Voss (Col. 1, lines 62-67) because the ability to achieve "extremely precise dosing" of an active agent onto the "pharmaceutical carrier" (reads on the instant delivery substrate) is possible only when one establishes the appropriate application parameters (such as nozzle size) in order to achieve the desired dosing and dissolution rate. The application

parameter inherently affects the deposition characteristics of the drops of bioactive agent onto the delivery substrate.

Therefore, the limitations of claims 1, 3-4, 8, 15, 18, 32-33, 38-46 and 49 are anticipated by the teachings of Voss.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 2, 5-7, 9-14, 16-17, and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Voss et al. (US 4,322,449) in view of Stimpson et al. (BioTechniques 25:886-890 November 1998).

The teaching of Voss with respect to extremely precise dose dotting of active pharmaceutical ingredients onto pharmaceutical carriers is stated above.

Voss does not expressly teach heating a solution including a bioactive agent with a thermal ejection element.

Stimpson discloses “a low-cost method to produce compact arrays using microporous materials and reagent jetting. Oligonucleotides are immobilized on membrane sheets as a series of lines” (Page 886, Abstract). “Jetting was carried out using piezoelectric (PZT) actuated delivery and thermal ink-jet printing" (Page 886, Materials and Methods section). An ink cartridge was disassembled; the ink sponge and ink removed, and 70μL of DNA solution were introduced into the entry port for the jet

head (Page 886, Materials and Methods section). “The lines of probe DNA were printed on Predator™ membrane (Pall Gelman Sciences, Port Washington, NY, USA)” (Page 887, left column). “About 200 lines of normal and mutant G551D probes were printed on opposite sides of the membrane using a thermal ink-jet” (Page 887, right hand column, and Figure 2). It is disclosed that the "thermal ink-jet approach appears to be a viable method of dispensing oligonucleotides" (Page 888, left hand column).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of extremely precise dose dotting of active pharmaceutical ingredients onto pharmaceutical carriers, as suggested by Voss, combine it with the thermal ink-jet method of dispensing active agents such as oligonucleotides, as suggested by Stimpson, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Stimpson teaches that "thermal ink-jet approach appears to be a viable method of dispensing oligonucleotides" (Page 888, left hand column) and Voss teaches the advantage of exact dosing by dotting active substances onto pharmaceutical carriers (Col. 6, lines 8-11).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claims 2, 12 and 37, the limitation of heating a solution including a bioactive agent with a thermal ejection element would have been obvious to one skilled in the art over the thermal ink-jet printing method disclosed by Stimpson for producing oligonucleotide arrays (Page 886, Materials and Methods section).

Regarding instant claims 5-7 and 35, the limitation of the volume of each of the drops would have been obvious to one skilled in the art over the discrete droplets of specific volume taught by Voss (Col. 1, line 62 to Col. 2, line 1). One skilled in the art would modify the process parameters such as nozzle size in order to achieve the desired droplet volume. The recited volumes would have been obvious variants during the process of routine optimization unless there is evidence of criticality or unexpected results.

Regarding instant claims 9 and 36, the standard deviation of drop volume of less than 15% of a mean drop volume would have been obvious to one skilled in the art over the discrete droplets of specific volume taught by Voss (Col. 1, line 62 to Col. 2, line 1). One skilled in the art would modify process parameters in order to reduce the standard deviation of the mean drop volume. The recited standard deviation would have been an obvious variant during the process of routine optimization unless there is evidence of criticality or unexpected results.

Regarding instant claims 10-11, 14, and 16-17, the selection of a second desired dot size would have been obvious to one skilled in the art over the discrete droplets of specific volume taught by Voss (Col. 1, line 62 to Col. 2, line 1) because during the

process of routine experimentation one skilled in the art would selecting a second dot size to have a different dissolution rate of the bioactive agent. One skilled in the art would also select a second dot size for an additional bioactive agent in the formulation that would be delivered by a different nozzle or jet or plurality of nozzles or jets.

Regarding instant claim 13, the limitation of the heated solution that is applied via at least two nozzles sized to eject drops of solution having substantially the same volume would have been obvious to one skilled in the art over the discrete droplets of specific volume taught by Voss (Col. 1, line 62 to Col. 2, line 1) because during the process of routine experimentation one would modify the process parameters in order to optimize the process efficiency. A method of increasing the process efficiency would be to add extra nozzles to provide faster dotting of bioactive agent onto the carrier.

Conclusion

10. No claims are allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615